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January 20, 2004
Date

Gina N. Shishima

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:
Yu

Serial No.: 09/841,720

Filed: April 24, 2001

For: MU OPIOID RECEPTOR METHODS

Group Art Unit: 1647

Examiner: Landsman, Robert S.

Atty. Dkt. No.: INDA:002USD1

I. AMENDMENT AND II. RESPONSE TO OFFICE ACTION DATED OCTOBER 20, 2003

Commissioner for Patents
P. O. Box 1450
Alexandria, VA 22313-1450

Commissioner:

This paper is submitted in response to the Office Action dated October 20, 2003 for which the date for response is January 20, 2004.

It is believed that no fee is due; however, should any fees under 37 C.F.R. §§ 1.16 to 1.21 be required for any reason, the Commissioner is authorized to deduct said fees from Fulbright & Jaworski L.L.P. Account No.: 50-1212/INDA:002USD1.

Reconsideration of the application is respectfully requested.

I. AMENDMENT

Please make the following amendments:

In the Title:

Please amend the title on page 1 (cover page) to read as follows: "Methods of Using Mu Opioid Receptors."

In the Claims:

1.-18. (Cancelled)

19. (Currently amended) A process for screening a candidate substance for its ability to bind to an opioid receptor comprising:

(a) providing a recombinant opioid receptor peptide or polypeptide encoded by a nucleic acid sequence comprising 25 contiguous nucleotides of SEQ ID NO:1;

(b) contacting the substance with the recombinant opioid receptor peptide or polypeptide; and

(c) detecting the ability of the candidate substance to bind to the recombinant opioid receptor peptide or polypeptide.

20. (Previously presented) The process of claim 18, wherein the nucleic acid sequence comprises 40 contiguous nucleotides of SEQ ID NO:1.

21. (Previously presented) The process of claim 19, wherein the nucleic acid sequence comprises 55 contiguous nucleotides of SEQ ID NO:1.

22. (Previously presented) The process of claim 20, wherein the nucleic acid sequence comprises 70 contiguous nucleotides of SEQ ID NO:1.

23. (Previously presented) The process of claim 21, wherein the nucleic acid sequence comprises SEQ ID NO:1.

24. (Previously presented) The process of claim 22, wherein the nucleic acid sequence comprises SEQ ID NO:1.

25. (Cancelled)

26. (Currently amended) The process of claim 20, wherein detecting the ability of the candidate substance to bind to the recombinant opioid receptor peptide or polypeptide

involves measuring (i) binding ability of the candidate substance to the recombinant opioid receptor peptide or polypeptide; (ii) the ability of the recombinant opioid receptor peptide or polypeptide to bind the candidate substance; (iii) ability of candidate to activate ion channels in a cell membrane; or (iv) modulation of ion channels in the cell membrane.

27. (Previously presented) The process of claim 20, wherein recombinant opioid receptor polypeptide is chimeric.

28. (Currently amended) A process for screening a candidate substance for its ability to bind to an opioid receptor comprising:

(a) expressing a recombinant opioid receptor peptide or polypeptide encoded by a nucleic acid sequence comprising 25 contiguous nucleotides of SEQ ID NO:1;

(b) contacting the candidate substance with the recombinant opioid receptor peptide or polypeptide; and

(c) detecting the ability of the candidate substance to bind to the recombinant opioid receptor peptide or polypeptide.

29. (Previously presented) The process of claim 27, wherein the nucleic acid sequence comprises 40 contiguous nucleotides of SEQ ID NO:1.

30. (Previously presented) The process of claim 27, wherein the nucleic acid sequence comprises 55 contiguous nucleotides of SEQ ID NO:1.

31. (Previously presented) The process of claim 27, wherein the nucleic acid sequence comprises 70 contiguous nucleotides of SEQ ID NO:1.

32. (Previously presented) The process of claim 27, wherein the nucleic acid sequence comprises SEQ ID NO:1.

33. (Cancelled)

34. (Previously presented) The process of claim 27, wherein recombinant opioid receptor polypeptide is chimeric.

35. (Currently amended) A process for screening a candidate substance for its ability to bind to [for an antagonist or agonist of] an opioid receptor comprising:

(a) providing a recombinant opioid receptor polypeptide comprising the amino acid residue sequence of SEQ ID NO:2;

(b) contacting the substance with the recombinant opioid receptor polypeptide; and

(c) detecting the ability of the candidate substance to bind to the recombinant opioid receptor polypeptide.

36. (Currently amended) The process of claim 34, wherein detecting the ability of the candidate substance to bind to the recombinant opioid receptor polypeptide involves measuring (i) binding ability of the candidate substance to the recombinant opioid receptor polypeptide; (ii) the ability of the recombinant opioid receptor polypeptide to bind the candidate substance; (iii) ability of candidate to activate ion channels in a cell membrane; or (iv) modulation of ion channels in the cell membrane.

37. (Previously presented) The process of claim 34, wherein the recombinant opioid receptor polypeptide is chimeric.

38. (New) The process of claim 34, further comprising determining whether the candidate substance is an agonist or antagonist.

In the specification:

Please replace the paragraph at page 2, line 1, with the following paragraph:

This application is a divisional of co-pending application Serial No. 08/120,601, filed July 13, 1993, which is a continuation-in-part of application 08/056,886, filed March 8, 1993.

Please replace the paragraph beginning at page 15, line 16, with the following:

In the drawings which form a portion of the specification it is shown ~~that~~ in ~~Figure 1~~ Figures 1A and 1B the amino acid sequence alignment of MOR-1, the mu opioid receptor, with the mouse δ-opioid receptor (DOR-1) (*Evans et al., 1992*) and the rat somatostatin receptors (SOM1 and SOM2) (*Meyerhof et al., 1991; Kluxen et al., 1992*). Seven hydrophobic domains are *underlined and numbered I to VII.* -, Amino acids identical to those in MOR-1. *Spaces*, gaps introduced for alignment, diamond figure, putative *N*-linked glycosylation sites; downward arrow, potential site for phosphorylation by CAMP-dependent protein kinase; O, potential sites for phosphorylation by protein kinase C; *, conserved aspartic acid residues proposed to interact with the amine group of ligands; =, conserved cysteine residues that might from a disulfide bond; ▾, potential palmitoylation site. The sequence for the MOR-1 cDNA has been submitted to GenBank (accession number L13069).

II. RESPONSE TO OFFICE ACTION

A. Status of the Claims

Applicant confirms that renumbering of the claims is proper and that claims 26 and 33 (as renumbered) were cancelled. Thus, claims 19-24, 26-32, and 34-37 were pending prior to the Office Action dated October 20, 2003. Claims 26, 35, and 36 have been amended. The amendments do not introduce new matter.

Applicant notes that the Action does not reject claims 23, 24, and 32, and thus, they appear allowable except for their dependency on a rejected claim.

B. Title

Without conceding any issue regarding the claimed invention, Applicant has amended the title of the application to recite "Methods of Using Mu Opioid Receptors," as requested by the examiner.

C. Figures

Applicant has amended the specification to make reference to FIG. 1A and 1B in accordance with the designation on the filed figures.

D. Claim Objections

Claim 24 has been amended to recite, "wherein the nucleic acid sequence encodes SEQ ID NO:2." Thus, it is not of similar scope as claim 23.

E. Amendment to Specification

Applicant has amended the specification to identify proper priority to an earlier filed application. The specification has been amended to recite: This application is a divisional of co-pending application Serial No. 08/120,601, filed September 13, 1993, which is a continuation-in-part of application 08/056,886, filed March 8, 1993. A copy of the inventor's Declaration that

was previously filed in this case as well as in the parent case is provided (Appendix A) as evidence that Applicant claimed priority to the identified application but that a clerical error was made in not properly amending the specification at the time this divisional application was filed. The Declaration identifies application 08/056,886, which was filed on March 8, 1993, and the amendment to the specification reflects this priority claim.

F. Claims 19-22, 26-31, and 34 Are Supported by an Adequate Written Description

The Action rejects claims 19-22, 26-31, and 34 under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. It contends that the claims contain subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors had possession of the claimed invention. More specifically, it argues that the claims are genus claims and that neither the specification nor the claims indicate what distinguishing attributes are shared by members of the genus. The Action alleges that the general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. The Action concludes that one skilled in the art cannot reasonably visualize or predict critical nucleic acid residues that would structurally characterize the genus of nucleic acids encoding the genus of opioid proteins claimed, because it is unknown and not described what structurally constitutes any different nucleic acids encoding an opioid receptor. As such, the Action concludes that the disclosure fails to provide a requisite number of species to describe the genus and, thus, Applicant was not in possession of the claimed invention as the time the invention was made. Applicant respectfully traverses this rejection.

The rejected claims are generally directed to a "process for screening a candidate substance for its ability to bind to an opioid receptor comprising: (a) [providing/expressing] a recombinant opioid receptor polypeptide encoded by a nucleic acid sequence comprising 25 contiguous nucleotides of SEQ ID NO:1; (b) contacting the substance with the recombinant opioid receptor polypeptide; and (c) detecting the ability of the candidate substance to bind to the recombinant opioid receptor polypeptide." Applicant respectfully points out that the claims are directed to screening processes involving peptides and polypeptides reciting the novel and nonobvious characteristics of the opioid receptor disclosed and that the rejections must be relevant to the claimed invention.

The Federal Circuit has stated that the test for the written description requirement is "whether the application relied upon 'reasonably conveys to the artisan that the inventor had possession at the time of the later claimed subject matter.'" *In re Daniels*, 144 F.3d 1452, 1456, 46 USPQ2d 1788, 1790 (Fed. Cir. 1998). See also *Markman v. Westview Instruments, Inc.* 52 F.3d 967, 34 USPQ 2d 1321 (Fed. Cir. 1995) (en banc) ("Claims must be read in view of the specification, of which they are a part."). In rejecting a claim under the written description requirement of 35 U.S.C. §112, first paragraph, the Examiner has the initial burden of presenting evidence or reasons why a person skilled in the art would not recognize in an applicant's disclosure a description of the invention defined in the claims. *In re Wertheim*, 541 F.2d 257, 262, 191 USPQ 90, 96 (CCPA 1976). Accordingly, the Examiner is required: (1) to set forth the claim limitation not described; and (2) to provide reasons why a person skilled in the art would not have recognized the description of the limitation in view of the disclosure of the application as filed. *Interim Guidelines for the Examination of Patent Applications Under 35 U.S.C. § 112, Paragraph 1*, Chisum on Patents, vol. 3, §7.04[1][c].

The Guidelines state that the "written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, *i.e.*, structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus." There are other ways to satisfy the requirement, but structure-function relationships clearly is contemplated. ***However, there is no stated requirement that the claims recite such relationships.*** Rather, the specification must merely support the relationship of structure to function.

Contrary to the Action's assertions that no structural attributes of genus members has been disclosed, the claim specifically recites specific structural limitations of the claimed peptides and polypeptides. They must be encoded by 25, 40, 55, or 70 contiguous nucleotides from SEQ ID NO:1. The specification fully discloses SEQ ID NO:1, and SEQ ID NO:2, which is the translated polypeptide encoded by SEQ ID NO:1. Consequently, a skilled artisan would recognize that the specification discloses ***thousands*** of species that meet the limitation of the claims. The specification fully support peptides and polypeptides that meet the limitations of the claims. Thus, the specification satisfies the written description requirement because it reasonably conveys to one of skill in the art that they had possession of the claimed subject matter. *In re Daniels*, 144 F.3d 1452, 1456, 46 USPQ2d 1788, 1790.

In accordance with the Federal Circuit's requirements pertaining to written description, one of ordinary skill in the art would have understood that Applicants were in possession of a screening method involving a recombinant opioid receptor peptide or polypeptide encoded by 25, 40, 55, or 70 contiguous nucleotides of SEQ ID NO:1.

The only remaining question, then, is whether there is a disclosed common function for the claimed peptides and polypeptides. Applicant directs the examiner to the discussion of antibody production set forth in the specification at pages 51-54. The claimed screening processes can employ fragments of SEQ ID NO:2 (encoded by contiguous nucleotides of SEQ ID NO:1) to screen antibodies directed to these polypeptides. Clearly, this is a function "common" to the claimed genus of polypeptides. Thus, under the Written Description guidelines, Applicant has provided a specific structure-function relationship that satisfies §112, first paragraph. And at this juncture, it should be beyond debate that a person of ordinary skill in the art would understand that the instant specification discloses thousands of different species with respect to SEQ ID NO:1 and SEQ ID NO:2, and that applicants thus possessed these different species. Thus, the specification satisfies the written description requirement because it reasonably conveys to one of skill in the art that they had possession of the claimed subject matter. *In re Daniels*, 144 F.3d 1452, 1456, 46 USPQ2d 1788, 1790.

The written description requirement has been extensively addressed by the Federal Circuit. In particular, the Federal Circuit has stated that "[t]he written description requirement does not require the applicant 'to describe exactly the subject matter claimed, [instead] the description must clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed.'" *Union Oil Co. of California v. Atlantic Richfield Co.*, 208 F.3d 989, 997, 54 USPQ 2d 1227, 1232 (Fed. Cir. 2000). The Federal Circuit has also noted that "[if] a

person or ordinary skill in the art would have understood the inventor to have been in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, then the adequate written description requirement is met." *In re Alton*, 76 F.3d 1168, 1175, 37 USPQ2d 1578, 1584 (Fed. Cir. 1996).

Regardless of what other components are added to those specifically provided, the full scope of the claimed invention was in possession of the inventors because the full scope of the invention is determined by the unique functional and structural characteristics of the compositions recited. In the present case, it is irrelevant whether additional sequences are attached to the compositions claimed as part of the methods because such additional sequences have not been claimed *per se*. If such a rejection were proper, "comprising" claim language could not be used with any claim, because in the case of nearly any composition or method it is possible to attach thereto some additional component of potentially unlimited size, which is itself not described in the application. What is relevant is that the claimed subject matter has been adequately *described* in a manner that reasonably conveys to one skilled in the art that the applicants were in possession of the invention and how to make and use the invention (which is discussed in the next section).

Moreover, a patentee does not need to describe every embodiment on which the claim reads. According to the Federal Circuit, "[i]t is well-established that a patent applicant is entitled to claim his invention generically, when he describes it sufficiently to meet the requirements of section 112." *Amgen v. Chugai Pharmaceutical Co.*, 927 F.2d 1200, 18 USPQ2D 1016, 1027 (Fed. Cir. 1991); *see also Utter v. Hiraga*, 856 F.2d 993, 998, 6 USPQ2D 1709, 1714 (Fed. Cir. 1988) ("A specification may, within the meaning of 35 U.S.C. §112, paragraph 1, contain a

written description of a broadly claimed invention without describing all species that claim encompasses.").

It is also noted that the examiner has not cited any legal precedent in support of this rejection. Unsurprisingly, that the Patent Office has regularly granted generic claims to polypeptides containing only small regions of homology with a polypeptide of interest, where few or no species are disclosed, is revealed by a cursory review of issued patents. For example, recently issued patents with just this situation include U.S. Patents 6,673,911; 6,660,839; 6,649,171; and 6,639,052. These 4 patents were identified in the first 28 out of 800 hits following a search of the U.S. PTO's website, using the claim terms "polypeptide" and "contiguous." In each case, generic claims were issued to peptides or polypeptides with only limited sequential identity to the referenced polypeptide, and where there was no discussion in the specification of retention of function as compared to the full length polypeptide. Thus, there clearly is no legal impediment to granting of such claims under this fact pattern.

The Examiner seems to be asserting that use of term "comprising" as the transitional phrase requires that all possible embodiments of the invention that the claim reads upon must be disclosed in the specification. By the Examiner's reasoning, for example, any claim to a polypeptide comprising a particular newly discovered amino acid sequence wherein the amino acid sequence is fully disclosed in the specification could never be claimed since it is possible that the amino acid sequence might at some later point in time be attached to an object that is not presently disclosed in the specification. Let us assume, for example, that this unknown object is a spaceship. Since the specification not only fails to disclose a spaceship, but fails to disclose how to construct a spaceship, then by the Examiner's logic there is no written description support in the specification for the polypeptide. This faulty logic used by the Examiner fails to take into

account the recited claim limitations. The claim limitations recite contiguous nucleotides from SEQ ID NO:1, which is fully described by the specification.

In the Examples disclosed in the Interim Guidelines, the explanation provided for Example 13 and protein variants indicates the rejected claims meet the requirements for written description. The first claim provided in Example 13 recites SEQ ID NO:3, which is said to satisfy the requirement because "each member of the genus shares SEQ ID NO:3 as a necessary common feature," contrary to the second claim in that example in which variants of SEQ ID NO:3 are claimed. With respect to the present case, each member of the claimed genus shares an amino acid sequence encoded by the recited portion of SEQ ID NO:1 as a "necessary common feature." Moreover, unlike the second claim in that example, there are common structural attributes that identify members of the genus, again, namely that they contain an amino acid sequence encoded by contiguous nucleotides of SEQ ID NO:1.

Accordingly, based on the arguments above, Applicant respectfully requests the rejection be withdrawn.

G. Claims 19-22, 26-31, and 34 Are Enabled

The Action rejects claims 19-22, 26-31, and 34 under 35 U.S.C. §112, first paragraph, as not providing enablement for methods of screening compounds for their ability to bind fragments of opioid receptors that are less than the full length of SEQ ID NO:1. The Action concedes that the application is enabling for methods of screening compounds for their ability to bind the opioid receptor SEQ ID NO:1. However, it argues that Applicant has provided no guidance or working examples of any functional opioid receptor less than the full length of SEQ ID NO:1. It further argues that Applicant has not taught which domains are responsible for ligand binding and receptor function as well as what amino acids would define an opioid receptor. The

examiner alleges that the claims recite an opioid receptor that can be as few as 25 contiguous bases of SEQ ID NO:1 (8 amino acids), and that it would not be predictable how to make a functional opioid receptor which is as few as 8 amino acids of SEQ ID NO:1. He further notes that the claims do not require that binding or functional domains be included. The Action then concludes that new experimentation would be required to practice the invention as claimed because Applicant has not provided any guidance or working example of structural, binding, or functional domains that make up opioid receptors, nor that it would be predictable to the skilled artisan in how to make a functional opioid receptor other than that of the full length of SEQ ID NO:1. Applicant respectfully traverses this rejection.

1. SEQ ID NO:2

Applicant notes that FIG. 1A identifies SEQ ID NO:2 as MOR-1, whose cloning from rat brain is described in Example I. Examples II and III show data generated using the cloned MOR-1 polypeptide. The specification provides relevant information regarding SEQ ID NO:1 and the cognate polypeptide, disclosed as SEQ ID NO:2. It shows that the cloned opioid receptor has binding activity and that it affects GTPase activity in a transfected cell. Specification at pages 138-142.

2. Legal Standard for Enablement

In examining a patent application, the PTO is required to assume that the specification complies with the enablement provisions of Section 112 unless it has "acceptable evidence or reasoning" to suggest otherwise. *In re Marzocchi*, 439 F.2d 220, 223-24, 169 USPQ 367, 369-370 (CCPA. 1971).

The PTO thus must provide reasons supported by the record as a whole what the specification is not enabling. *Application of Angstadt*, 537 F.2d 498, 504, 190 USPQ 214, 219-220 (CCPA 1979). Then and only then does the burden shift to the applicant to show that one of ordinary skill in the art could have practiced the claimed invention without undue experimentation. *In re Strahilevitz*, 668 F.2d. 1229, 1232, 212 USPQ 561, 563-64 (CCPA 1982) (emphasis supplied.). In this case, no references or evidence has been cited to support the enablement rejection.

Furthermore, the *Wands* factors are identified but the applicability of only some of these factors to this case are discussed, and even these are misguided. For example, the examiner focuses on the need for a functional receptor. As discussed above in the response to the written description rejection, there is no limitation implicit or explicit in the claims that there be a functional receptor. Also, there is a flaw with the instant rejection in assuming that the ***only*** utility for the peptides and polypeptides of the instant claims is that must encode a functional mu opioid receptor. Binding to a polypeptide can occur whether or not that polypeptide is functional in its usual context. Much to the contrary, §112, first paragraph, requires only that there be ***some*** way to make and use the claimed subject matter. As described in the specification at page 13, lines 6-21, there is an enabled use of even non-functional fragments of a mu opioid receptor for the production of anti- mu opioid receptor antibodies. In the absence of some reason why one of skill in the art could not readily employ the claimed peptides and polypeptides in the production of such antibodies, enablement has been established.

In light of the examiner's misreading of the claims to require a functional receptor, and the subsequent arguments based on that misreading, Applicant urges this rejection be withdrawn.

H. Claims Satisfy 35 U.S.C. §112, Second Paragraph

1. Claims 26 and 36 Are Definite

The Action rejects claims 26 and 36 under 35 U.S.C. §112, second paragraph, as being indefinite. Claims 26 and 36 have been amended as follows:

> The process of claim [20 or 34], wherein detecting the ability of the candidate substance to bind to the recombinant opioid receptor polypeptide involves measuring (i) binding ability <u>of the candidate substance to the recombinant opioid receptor polypeptide</u>; (ii) the ability of the recombinant opioid receptor polypeptide to bind the candidate substance; (iii) ability of candidate to activate ion channels in a cell membrane; or (iv) modulation of ion channels in the cell membrane.

The amendment clarifies that "detecting the ability of the candidate substance to bind to the recombinant opioid receptor polypeptide" can be accomplished by measuring the binding ability of the candidate substance to the recombinant opioid receptor polypeptide or of the recombinant receptor polypeptide to the candidate substance.

The Action also rejects these claims for reciting that the ability of the candidate substance to bind to the recombinant opioid receptor polypeptide can be detected by measuring "ability of candidate to activate ion channels in a cell membrane; or (iv) modulation of ion channels in the cell membrane." It alleges that these are functional assays and that they do not necessarily demonstrate the candidate substances bind to the polypeptide.

However, the specification indicates that with screening processes of the invention, "it is generally desirable to employ a system wherein one can measure the ability of the receptor polypeptide to bind to and or be modified by the effector employed in the presence of a particular substance." Specification at page 63, lines 20-26. It also indicates in the background that these

receptors are typically part of receptor/transmembrane system that involves an effector, such as an ion channel. Specification at page 4, lines 8-12. A person of ordinary skill in the art would recognize that one way to evaluate whether a candidate substance bound to a recombinant opioid receptor polypeptide is to measure a downstream event, such as activation of ion channels in a cell membrane or modulation of ion channels in the cell membrane. Consequently, the claims are clear. Applicant respectfully requests this rejection be withdrawn.

2. Claims 28-32 and 34 Are Complete

The Action rejects claims 28-32 and 34 as being incomplete for omitting essential steps. More specifically, it contends that the only difference between claims 28-32 and 34 from claims 19-24, 26, and 27 is that the first set has the limitation "expressing" which the second set has the recitation "providing." Consequently, the Action contends that claim 28 should add a limitation that DNA is transfected into a cell. Applicant respectfully traverses this rejection.

Applicant acknowledges that claim 28 recites "expressing a recombinant opioid receptor polypeptide" while claim 19 recites "providing a recombinant opioid receptor polypeptide." However, the examiner is incorrect in asserting that claim 28 therefore requires a limitation that DNA is transfected into a cell. There are numerous ways to express a recombinant polypeptide in addition to transfecting DNA into a cell. For example, a protein can be expressed using a cell lysate such as a rabbit reticulocyte system or it can be expressed from a cell that has been infected with a virus, which may be a DNA or RNA virus. Moreover, claim 28 is clear as written. Applicant does not wish to limit the claim as suggested by the examiner because there is no need for the limitation. Applicant respectfully requests this rejection be withdrawn.

3. Claims 35-37 Are Complete

The Action rejects claims 35-37 as incomplete, contending that a step for determining whether an agent is an agonist or antagonist is required. Claim 35 has been amended to recite:

> A process for screening a candidate substance for its ability to bind to an opioid receptor comprising:
>
> (a) providing a recombinant opioid receptor polypeptide comprising the amino acid residue sequence of SEQ ID NO:2;
>
> (b) contacting the substance with the recombinant opioid receptor polypeptide; and
>
> (c) detecting the ability of the candidate substance to bind to the recombinant opioid receptor polypeptide.

The amendment renders the rejection moot. Consequently, Applicant respectfully requests this rejection be withdrawn.

I. Double Patenting Rejection Is Improper

The Action rejects claim 19-24, 26-32, and 34-36 under 35 U.S.C. §101 as claiming the same invention as that recited in co-pending Application No. 09/626,616 (INDA:005USD1). The examiner noticed that both applications are drawn to methods of screening opioid compounds. However, he was unable to examine the cited application further as it was unavailable at the time of this Office Action.

As this is a provisional rejection, Applicant will address the rejection once the claims are otherwise allowable, if necessary.

J. Claims Are Not Anticipated by the Cited References

1. Claims 19-22, 26, 28-31, 35, and 36 are not Anticipated by Chen *et al.*

The Action rejects claims 19-22, 26, 28-31, 35, and 36 under 35 U.S.C. §102(a) as being anticipated by Chen *et al.*[1] ("Chen"). It contends that Chen teaches methods of screening candidate substances using the recited opioid receptor. Applicant respectfully traverses this rejection.

As discussed in the priority application (Paper 9 in 08/120,601), the Chen reference is not prior art to the present invention:

> The instant application [08/120,601] is a continuation-in-part application of co-pending application Serial No. 08/056,886, filed on March 8, 1993. This paper [Chen] was published on behalf of Lei Yu after the initial filing date of the parent application and is, therefore, not available as prior art. In order to traverse this rejection, Applicant files a Declaration of Lei Yu.

A copy of the Declaration of Lei Yu is included herewith (Appendix A). This Declaration demonstrates that the authors of Chen, other than Lei Yu, are not inventors of the claimed subject matter. These non-inventor authors were researchers in Dr. Yu's laboratory. Under the direction and control of Dr. Yu, they performed tasks related to the creation of the claimed subject matter. They did not participate in the conception of the claimed subject matter, as disclosed in the Declaration. Consequently, the Chen reference is not a prior art reference under 35 U.S.C. § 102(a). Applicant respectfully requests this rejection be withdrawn.

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[1] The Action states that the claims are anticipated by Evans *et al.* (U. S. Patent No. 6,265,563). However, later in that same rejection, the reference of Chen *et al.* is cited and in the next rejection, Evans is cited. Therefore, Applicants assume the first 102 rejection was based on the Chen *et al.* reference.

2. Claims Are Novel over Evans *et al.*

The Action rejects claims 19-22, 26, and 28-31 under 35 U.S.C. §102(e) as being anticipated by Evans *et al.* (U. S. Patent No. 6,265,563) ("Evans"). More specifically, it contends that Evans teaches methods of teaching candidate substances for their ability to bind an opioid receptor comprising at least 25 contiguous bases of SEQ ID NO:1. It refers to sequence comparison B and columns 18-19 in the patent. Applicant respectfully traverses this rejection.

"A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 U.S.P.Q.2d 1051, 1053 (Fed. Cir. 1987). The Evans reference does not teach each element of the rejected claims.

Independent claims 19 and 28 recite:

19. A process for screening a candidate substance for its ability to bind to an opioid receptor comprising:
    (a) providing a recombinant opioid receptor polypeptide encoded by a nucleic acid sequence comprising 25 contiguous nucleotides of SEQ ID NO:1;
    (b) contacting the substance with the recombinant opioid receptor polypeptide; and
    (c) detecting the ability of the candidate substance to bind to the recombinant opioid receptor polypeptide.

28. A process for screening a candidate substance for its ability to bind to an opioid receptor comprising:
    (a) expressing a recombinant opioid receptor polypeptide encoded by a nucleic acid sequence comprising 25 contiguous nucleotides of SEQ ID NO:1;
    (b) contacting the candidate substance with the recombinant opioid receptor polypeptide; and
    (c) detecting the ability of the candidate substance to bind to the recombinant opioid receptor polypeptide.

The Evans reference does not teach a process for screening that involves "detecting the ability of the candidate substance to bind to" a "polypeptide encoded by a nucleic acid sequence

comprising 25 contiguous nucleotides of SEQ ID NO:1," contrary to the Action's reliance on Sequence Comparison B and columns 18-19 in the patent. Sequence Comparison B shows only a sequence alignment between SEQ ID NO:1 and the clone DOR-2. Columns 18-19 concern clone DOR-1, which the Evans patent states is a gene that is ***different*** than DOR-2 (see col. 22, lines 47-48). Thus, the patent does not teach any screening methods with respect to DOR-2, the sequence for which the alignment is shown.

Moreover, the alignment in Sequence Comparison B does not identify any region or DOR-2 that has 70 contiguous nucleotides of SEQ ID NO:1. Thus, the limitations of claims 22 and 31 are not met.

Furthermore, if an art rejection based on this reference is to be maintained, Applicant requests that a copy of the priority document for the Evans patent (Serial No. 07/929,200 filed on Aug. 13, 1992) be provided.

K. Claims Are Nonobvious

1. Claims 27 and 34 Are Nonobvious over Evans in View of Xie *et al.*

The Action rejects claims 27 and 34 under 35 U.S.C. §103(a) as being unpatentable over Evans in view of Xie *et al.* ("Xie"). The Action states that Evans does not teach opioid chimeras, but that Xie does teach opioid chimeras. The Action concludes that it would have been obvious for one of ordinary skill in the art at the time of the present invention to have made opioid chimeras using the opioids of Evans and the method of Xie in order to further characterize the binding and functional characteristics of the proteins of Evans.[2] It also argues that there is a

[2] The Action intended to say "It would have been obvious to one of ordinary skill in the art at the time of the present invention to have made an opioid chimera using the opioid of Xie and the method of Evans in order to further characterize the binding and functional characteristics of the protein of Xie."

reasonable expectation of using the proteins since recombinant techniques were well-known and highly successful in the art at the time of the present invention. Applicant respectfully traverses this rejection.

To establish a proper *prima facie* case of obviousness, "the prior art reference (or references when combined) must teach or suggest all the claim limitations." MPEP §2142. As discussed above, Evans does not teach the claimed methods. Furthermore, the Xie reference does not address this deficiency because it does not teach the claimed method as well.

Moreover, the Xie reference does not, contrary to the assertion in the Action, teach the limitation recited in rejected claims 27 and 34. These claims recite, "wherein the recombinant opioid receptor is chimeric." Xie describes chimeric opioid peptides—***ligands*** for the receptors, not the receptors themselves. The title of the paper ("Chimeric opioid peptides: Tools for identifying opioid receptor types") and the abstract ("We synthesized several chimeric peptides in which the N-terminal nine residues of dynorphin-32—a peptide selective for the κ opioid receptor, were replaced by opioid peptides selective for other opioid receptor types") make this clear. Therefore, because all of the claim recitations are not taught by the combination of Evans and Xie, a proper *prima facie* case has not been made. Applicant respectfully requests this rejection be withdrawn.

2. Claims 27 and 34 Are Nonobvious over Chen in View of Xie

The Action rejects claims 27 and 34 under 35 U.S.C. § 103(a) as being unpatentable over Chen in view of Xie for the same reasons as discussed above. Applicant respectfully traverses this rejection.

As discussed earlier, the Chen reference is not proper prior art. Furthermore, the Xie reference does not teach a recombinant chimeric opioid receptor. Therefore, all of the limitations

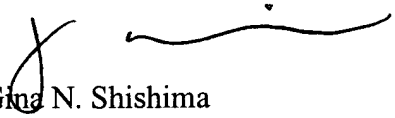
of the claims are not met by this combination of references. Accordingly, Applicant respectfully requests this obviousness rejection be withdrawn.

CONCLUSION

Applicant believes that the foregoing remarks fully respond to all outstanding matters for this application. Applicant respectfully requests that the rejections of all claims be withdrawn so they may pass to issuance.

Should the Examiner desire to sustain any of the rejections discussed in relation to this Response, the courtesy of a telephonic conference between the Examiner, the Examiner's supervisor, and the undersigned attorney at 512-536-3081 is respectfully requested.

Respectfully submitted,



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